Detection of aortic graft infection by fluorodeoxyglucose positron emission tomography: Comparison with computed tomographic findings

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Objective: **Radionuclide imaging with fluorodeoxyglucose (FDG) and positron emission tomography (PET) has been proposed for the identification of vascular graft infection; however, its accuracy has not been determined. We performed this prospective study to compare the usefulness of FDG-PET in the assessment of vascular graft infection relative to computed tomography (CT).**

Methods: **FDG-PET was performed for 33 consecutive patients with a suspected arterial prosthetic graft infection. The PET images were then assessed visually in terms of the density of uptake. In cases with positive uptake, the pattern of accumulation was also defined, such as focal or diffuse uptake. We compared the diagnostic efficiency of PET with contemporaneous CT in detection of infection of the arterial prosthetic graft.**

Results: **On the basis of the surgical, microbiological, and clinical follow-up findings, the aortic grafts were considered infected in 11 patients and not infected in 22 patients. Although the sensitivity of PET (91%) was higher than that of CT (64%), its specificity (64%) was lower than that of CT (86%). When focal uptake was set as the positive criterion in FDG, the specificity and positive predictive value of PET for the diagnosis of aortic graft infection improved significantly to 95% ($P < .05$ for both).**

Conclusions: **Although both techniques are useful in evaluation of patients with suspected aortic graft infection, using the characteristic FDG uptake pattern described previously as a diagnostic criterion made the efficacy of FDG superior to that of CT in the diagnostic assessment of patients with suspected aortic graft infection. (J Vasc Surg 2005;42:919-25.)**

Aortic prosthetic graft infection is associated with high morbidity and mortality in the absence of immediate, definitive antibiotic therapy and surgical intervention.[1] Computed tomography (CT) has been used as a complementary imaging approach for the assessment of graft infection, because the high spatial resolution of CT provides exquisite detail of the vascular structure and perivascular spaces. However, hematomas and seromas in the vicinity of a vascular graft appear anatomically similar to an abscess, thus making it sometimes difficult to distinguish between noninfected and infected prosthetic grafts on CT images.[2] Thus, a reliable physiological approach is required to evaluate the inflammatory activity, to detect infected prostheses, and to determine the extent of infection, in addition to anatomic information.

Investigators have recently suggested that fluorodeoxyglucose (FDG) positron emission tomography (PET) imaging may be useful for detection of infection[3,4] and evaluation of infected vascular grafts.[5-7] However, because the vascular graft regions can exhibit a substantial inflammatory reaction that results in some FDG accumulation,[8] the value of FDG-PET in the assessment of vascular graft infection is still ambiguous. We hypothesized that PET, because of its ability to detect inflammation, would be a more sensitive and specific test for aortic graft infection. To clarify this issue, we conducted this preliminary study to examine the feasibility of using FDG-PET for the diagnosis of aortic graft infection in comparison with CT.

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Competition of interest: none.

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METHODS

Patient recruitment. This study was a prospective analysis of consecutive patients undergoing combined FDG-PET and CT between September 2002 and November 2004 in National Cardiovascular Center Hospital. Thirty-three patients who underwent aortic reconstructive surgery with grafting for the treatment of aortic aneurysm, aortic dissection, or aortoiliac occlusive disease (mean age, 71 ± 14 years [mean ± SD]; age range, 22-83 years) were enrolled in the study. These patients were categorized into three groups according to the criteria of Fiorani et al.[9] Nine patients had suspected advanced aortic graft infection with manifestations of severe infection, 17 had suspected low-grade aortic graft infection with nonspecific manifestations of infection, and 7 were asymptomatic control patients selected from a review of patients at our institution who had undergone FDG whole-body PET mainly for oncologic purposes dur-

Table I. Patient characteristics

Patient No.	*Age/sex*	*Primary disease*	*Type of operation*	*Final diagnosis*	*Proof of infection*	*CT findings*	*PET findings*
1	75/M	AAA	Y-graft	Infection	ST	TP	TP
2	74/M	TAA	TAR	Infection	MF	FN	TP
3	80/M	AAA	I-F bypass	Infection	ST	TP	TP
4	62/M	TAA	TAR	Infection	ST	FN	TP
5	78/M	AAA	Y-graft	Infection	ST	TP	TP
6	83/F	IA	TAR	Infection	ST	FN	TP
7	83/M	AAA	Y-graft	Infection	MF	TP	TP
8	74/M	TAA	TAR	Infection	MF	FN	TP
9	22/M	AE	Ascending graft	Infection	MF	TP	TP
10	31/M	AD	TAR	Infection	CF	FN	TP
11	80/M	TAA	TAR	Infection	CF	TP	TP
12	75/M	IA	S-graft	NEI	CF	TN	TN
13	70/M	AAA	Y-graft	NEI	AsC	TN	FP
14	77/F	AAA	Y-graft	NEI	AsC	TN	TN
15	77/M	AAA	Y-graft	NEI	CF	TN	TN
16	75/M	AAA	A-F bypass	NEI	CF	TN	TN
17	64/M	AAA	Y-graft	NEI	ST	FP	TN
18	82/F	AAA	S-graft	NEI	AsC	TN	TN
19	83/M	TAA	TAR	NEI	ST	FP	TN
20	73/M	AAA	Y-graft	NEI	CF	TN	TN
21	63/M	AAA	Y-graft	NEI	AsC	TN	FP
22	66/M	AAA	Y-graft	NEI	CF	TN	TN
23	72/M	AAA	Y-graft	NEI	CF	TN	FP
24	76/M	AAA	Y-graft	NEI	AsC	TN	FP
25	75/M	AAA	Y-graft	NEI	CF	FP	TN
26	68/F	AAA	A-F bypass	NEI	AsC	TN	FP
27	80/M	AAA	Y-graft	NEI	ST	TN	TN
28	76/M	AAA	Y-graft	NEI	CF	TN	FP
29	83/M	TAA	Descending graft	NEI	CF	TN	TN
30	75/M	AD	Descending graft	NEI	CF	TN	TN
31	49/M	TAA	Descending graft	NEI	ST	TN	TN
32	82/M	TAA	TAR	NEI	AsC	TN	FP
33	72/M	TAA	Descending graft	NEI	CF	TN	FP

CT, Computed tomography; *PET,* positron emission tomography; *AAA,* abdominal aortic aneurysm; *I-F,* iliofemoral; *ST,* surgical treatment; *TP,* true positive; *TAA,* thoracic aortic aneurysm; *TAR,* total arch replacement; *MF,* microbiological findings; *FN,* false negative; *IA,* infected aneurysm; *AE,* annuloaortic ectasia; *AD,* aortic dissection; *S-graft,* straight graft; *NEI,* no evidence of infection; *TN,* true negative; *CF,* clinical feature; *AsC,* asymptomatic controls; *FP,* false positive.

ing the same period. The final diagnosis was based on the surgical and microbiological findings. In cases in which no surgical treatment or no microbiologic samples were available, clinical follow-up for more than 4 months served as the standard reference. Twenty-five patients had received some antibiotic therapy before the FDG-PET and CT study, but the drugs were not changed until after both imaging studies. Patients with diabetes mellitus were excluded from the study because this condition can affect the FDG uptake.[10] This study was conducted with the approval of our institutional review board, and we obtained written informed consent from all the subjects before their participation in the study.

CT protocol. CT scanning was conducted within 1 week before FDG-PET by using a helical or multidetector CT system (Aquilion; Toshiba Medical Co, Tochigi, Japan). Contiguous 1-cm sections were obtained at 1-cm intervals from the lung apices to the inguinal region after bolus intravenous injection of contrast material, except in four patients with acute or chronic renal failure.

PET protocol. Patients were instructed to fast for at least 5 hours before FDG-PET studies. Transmission scans were initially obtained by using a line source of germanium 68/gallium 68, and then 185 MBq of FDG was administered intravenously. One hour later, emission from the entire body was imaged for 25 minutes; at least five bed positions were used. The emission data obtained from the ECAT EXACT 47 (Siemens/CTI, Knoxville, Tenn) were consecutively reconstructed with measured attenuation correction based on the transmission data.

Image interpretation. All the CT scans were reviewed independently by two of the authors, who had no knowledge of the clinical or operative findings. In accordance with a previously described method,[11] each CT scan was assessed for the presence of ectopic gas, perigraft fluid (<20 Hounsfield Units), perigraft soft tissue (>20 Hounsfield Units), pseudoaneurysm formation, discontinuity of the aneurysmal wrap, and an increased amount of soft tissue (>5 mm) between the graft and the

Table II. Demographic data of patients with and without aortic graft infection

Variable	*Group*		P *value*
	With infection	*Without infection*	
Age (y)	68 ± 21	73 ± 8	NS
Sex (F/M)	1/10	3/19	NS
Smoking	7/11 (64%)	15/22 (68%)	NS
CRP (mg/dL)	5.6 ± 5.0	3.5 ± 4.5	NS
FBS (mg/dL)	100 ± 10	97 ± 14	NS
Duration (mo)	11.8 ± 9.4	12.5 ± 9.2	NS
Location of graft (thorax/abdomen)	7/4	6/16	.04

Data are n (%) or mean ± SD.
CRP, C-reactive protein; *FBS,* fasting blood sugar; *NS,* not significant.

surrounding aneurysmal wrap. If the interpretations of the observers disagreed, a consensus of the two observers was obtained.

The FDG-PET images were analyzed by two independent experienced physicians who specialized in nuclear medicine and who were blinded to the results of the other imaging studies. They used the same image-evaluation criteria as those used in a previous FDG-PET study for detection of orthopedic infection.[12] The intensity of FDG uptake was graded on a five-point scale, as follows: grade 0, FDG uptake similar to that in the background; grade 1, low FDG uptake, comparable to that by inactive muscles and fat; grade 2, moderate FDG uptake, clearly visible and distinctly higher than the uptake by inactive muscles and fat; grade 3, strong FDG uptake, but distinctly less than the physiologic uptake by the bladder; and grade 4, very strong FDG uptake, comparable to the physiologic urinary uptake by the bladder. In a previous investigation by Stumpe et al,[12] the results of a receiver operating characteristic analysis had shown that classifying lesions with grade 3 or 4 uptake as infected lesions yielded the best discrimination between infected and noninfected lesions. Therefore, increased grade 3 or 4 FDG uptake by a prosthesis was used as the diagnostic criterion for infection in our study. In addition, in cases showing abnormal FDG uptake, the readers also described the pattern of abnormal uptake, namely, whether it was focal or diffuse. An abnormality was interpreted as diffuse if it was located along the prosthesis consecutively. An abnormality was called focal if it was located in a region other than along the prosthesis and was dotted in configuration.

Statistical analysis. Data are expressed as means ± SD. The interobserver agreement of image interpretation was estimated by using the κ statistic.[13] Concordance was considered to be good for κ values more than 0.6, moderate for values from 0.6 to 0.4, and poor for values less than 0.4.[14] Comparisons between groups were conducted by using the unpaired *t* test for continuous variables. The diagnostic performance was expressed in terms of the sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV), with 95% confidence intervals. Differences in the diagnostic performance between the two imaging modalities and criteria were considered significant when the 95% confidence intervals did not overlap.[15]

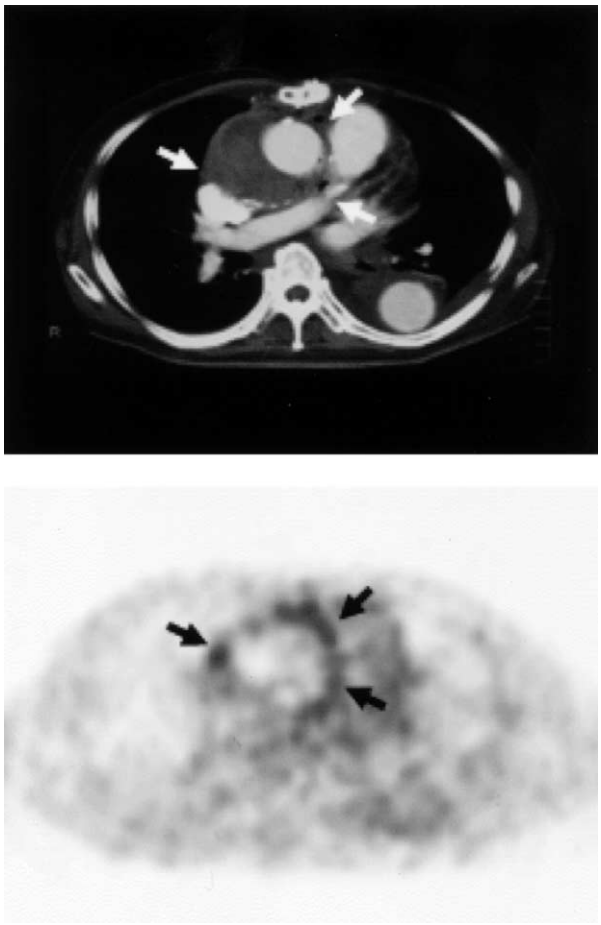

Fig 1. Example of true-positive findings on computed tomography (CT) and fluorodeoxyglucose (FDG) positron emission tomography in a patient with graft infection. The patient had undergone total aortic arch replacement 4 months before the imaging examinations. Focal FDG accumulation in the graft *(black arrows)* is accompanied by fluid collection and extraluminal air on the enhanced CT image *(white arrows)*.

RESULTS

The characteristics of patients and the results of imaging are presented in Table I. Eleven of 33 patients were definitively categorized as having infected grafts on the basis of the surgical procedure, including graft removal, aortic ligation, and extra-anatomic bypass grafting (n = 5), and microbiological findings, including blood culture and follow-up imaging studies (n = 6). Another 22 patients were definitively categorized in the noninfected-graft group. There were no significant differences between the two groups in the patients' mean age, sex distribution, history of smoking, serum C-reactive protein, or blood

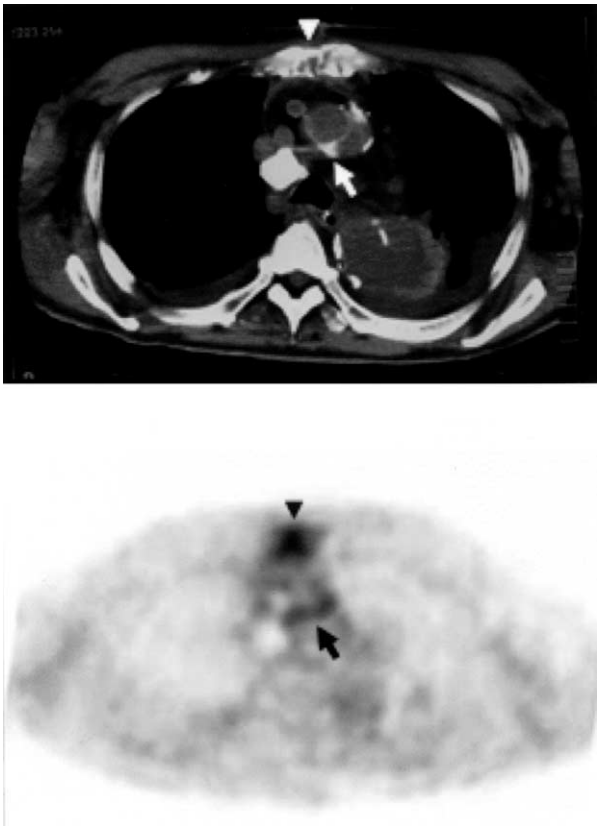

Fig 2. Example of a false-negative computed tomography (CT) result and true-positive fluorodeoxyglucose (FDG) positron emission tomography (PET) findings in a patient with graft infection. The patient had undergone total aortic arch replacement 4 months before the imaging examinations. Focal FDG accumulation in the ascending aortic graft *(black arrow)* is seen in the FDG-PET image, but only soft tissue swelling is seen in the plain CT image *(white arrow)*. Physiological FDG accumulation was also seen at the site of sternotomy *(arrowhead)*.

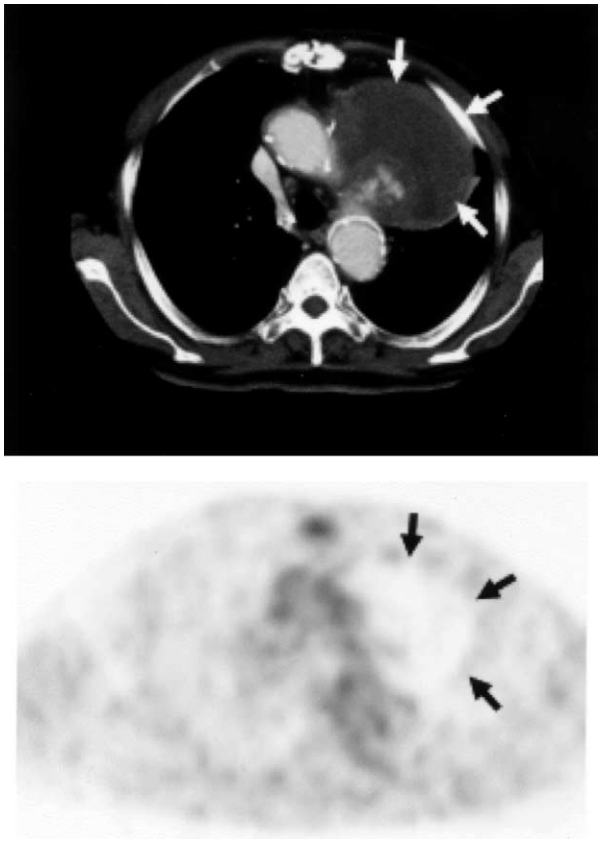

Fig 3. Example of false-positive findings on computed tomography (CT) and a true-negative result on fluorodeoxyglucose (FDG) positron emission tomography in a patient without graft infection. An exophytic perigraft fluid density is seen *(white arrows)* at the prosthetic aortic arch on a contrast-enhanced CT image. At this site, there is no accumulation of FDG at all *(black arrows)*.

sugar at the time of the PET study or during follow-up after surgery. However, the incidence of infection in thoracic aortic grafts was significantly higher than that in abdominal grafts (Table II).

Regarding the interpretation of CT images, the interobserver agreement on positive observations was 0.85, and the κ value was 0.67. CT revealed true-positive findings in 7 cases and false-positive findings in 3, and it showed a true-negative result in 19 and a false-negative result in 4.

All FDG-PET images were considered appropriate for interpretation. Interobserver agreement on positive observations was 0.82, and the κ value was 0.61. FDG-PET showed true-positive findings in 10 cases and false-positive findings in 8, and it showed a true-negative result in 14 and a false-negative result in one. All patients with true-positive findings on CT also showed increased FDG uptake by the corresponding lesions (Fig 1). Additionally, in all cases with false-negative CT findings, FDG-PET could depict the lesions as positive (Fig 2). Only one patient with false-positive CT findings underwent reoperative irrigation, and the preoperative FDG-PET result in that patient was completely negative (Fig 3). Histopathologic assessment of the resected specimen also confirmed that the perigraft mass represented noninfected sterile fluid in that case. FDG-PET showed positive findings of infection, based on the visual assessment criteria, in eight patients without graft infection. In these patients with false-positive FDG findings, the FDG uptake grade differed, but the pattern of uptake was diffuse and circumferential around the prosthetic graft in all cases (Fig 4).

On the basis of these data, the sensitivity, specificity, PPV, NPV, and accuracy of CT for the diagnosis of graft infection were 64%, 86%, 70%, 83%, and 79%, respectively. The corresponding values for FDG-PET were 91%, 64%, 56%, 93%, and 73%, respectively. The sensitivity of FDG-PET (91%) was significantly higher than that of CT (64%; $P < .05$); however, the specificity of FDG-PET (64%) was lower than that of CT (86%; not significant). When the PET criterion for infection was defined as focal abnormal uptake with respect to the characteristics of false-positive

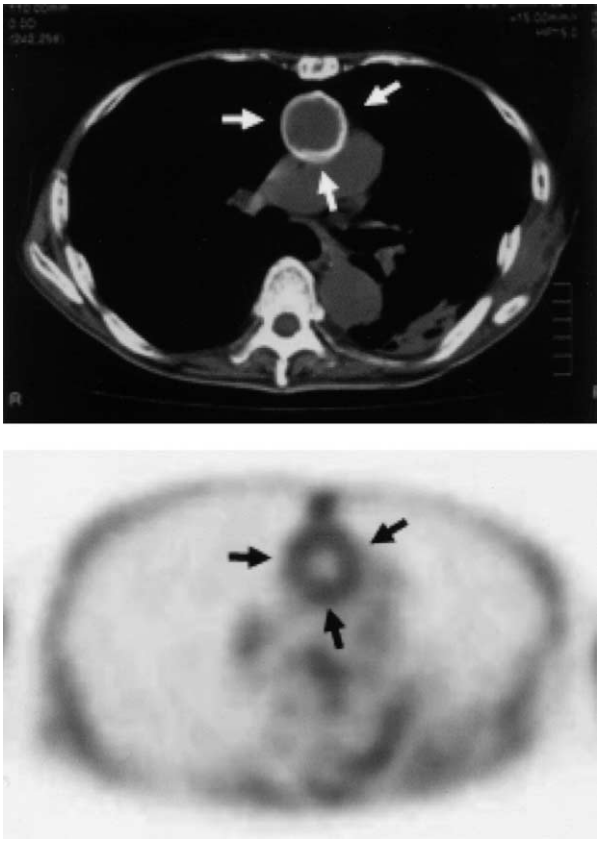

Fig 4. Example of a true-negative computed tomography (CT) result and false-positive fluorodeoxyglucose positron emission tomography (FDG-PET) findings in a patient without graft infection. The prosthetic aortic graft can be seen as a high-density rim around the ascending aortic region on CT *(white arrows)*. The FDG-PET image depicts a relatively dense and diffuse uptake around the graft *(black arrows)*.

FDG uptake, all the false-positive cases were categorized as negative. With this alteration of the diagnostic criteria, the specificity and PPV of FDG-PET improved significantly from 64% to 95% and 56% from 91%, respectively ($P < .05$). An overview of the diagnostic performance of CT and of FDG using the two methods of assessment, as well as the 95% confidence intervals, is shown in Table III.

DISCUSSION

Because infection of aortic prosthetic grafts remains a major surgical challenge, it is essential for aortic graft infection to be diagnosed accurately and safely.[1,2] CT and scintigraphic techniques are currently the most commonly used modalities for diagnosis of aortic graft infection.[2] Because of the rapidity with which it can be performed, CT should be the first examination ordered in cases of suspected aortic graft infection. Studies of the early 1980s have showed specificity and sensitivity of CT of approximately 100%.[16] However, studies of the late 1980s, which included cases with low-grade infection, indicated an overall diagnostic sensitivity of 55.5% and an overall diagnostic specificity of 100% of CT for graft infection.[9] This imaging modality was considered an accurate method for diagnosis of advanced graft infection (periprosthetic abscess, aortoenteric fistula, and so on), but the risk of false-negative results is high in cases with low-grade graft infection. In this study, CT failed to identify three cases with aortic graft infection; consequently, the sensitivity of CT for the diagnosis of aortic graft infection decreased to 64%. Thus, it would be desirable to identify another imaging modality, besides CT, with a high sensitivity for detecting aortic graft infection.

Whereas CT affords visualization of the structural changes secondary to infection, nuclear medicine techniques allow such infections to be diagnosed on the basis of molecular biological changes.[2] Although several types of scintigraphic techniques have been used for many years, FDG-PET has drawn much attention recently for diagnosis of infectious diseases. Previous articles have shown that FDG-PET can be a very sensitive imaging modality for diagnosis of infection,[3,4] because increased FDG uptake is observed in the activated inflammatory cells, such as leukocytes, granulocytes, and macrophages.[17] Although some case reports have been published,[5-7] the usefulness of FDG-PET in the diagnosis of aortic graft infection has not yet been evaluated on sufficiently large numbers of patients.

This study confirmed the feasibility of FDG-PET for detecting aortic graft infection. As compared with the conventional nuclear medicine techniques, PET is considered to have the following advantages.[4] First, the PET procedure is much faster than the conventional modalities, and its results can usually be made available within 2 hours. Second, the better spatial resolution of the PET system as compared with that of a gamma camera results in a higher diagnostic sensitivity. Third, PET generally provides higher-quality images with superior contrast compared with single photon emission CT. Thus, FDG-PET can be used to assess the extent of infection more sensitively and can quantify the inflammatory activity more accurately than a gamma camera. The superiority of FDG-PET compared with other gamma camera techniques has been confirmed in oncology, but not yet in infectious disease.[18,19] Unfortunately, we could not compare FDG-PET with the conventional gamma camera imaging modalities in this study, but the above-mentioned advantages suggest that FDG-PET has the possibility to replace them as a diagnostic tool for patients with suspected aortic graft infection.

Although the ability of FDG-PET to diagnose several types of infection with a high sensitivity has been encouraging, high sensitivity inevitably means a certain number of false-positive results.[4] Previous reports indicated that prosthetic vascular graft replacement was sometimes associated with a false-positive FDG uptake in the graft or stent regions.[8,20] Our visual FDG-PET analysis also showed a false-positive accumulation in 8 (36%) of 22 patients with noninfected grafts. This false-positive accumulation might be explained as FDG uptake during the process of normal foreign body reaction or inflammation during the normal

Table III. Diagnostic performances of CT and FDG-PET for differentiation between infected and noninfected vascular grafts

Variable	*CT findings*	*Visual assessment of FDG-PET*	
		Positive/negative	*Focal/not*
Sensitivity	0.64 (0.48-0.80)	0.91 (0.81-1.00)*	0.91 (0.81-1.00)*
Specificity	0.86 (0.74-0.98)	0.64 (0.48-0.80)	0.95 (0.88-1.02)†
Accuracy	0.79 (0.65-0.93)	0.73 (0.58-0.88)	0.94 (0.86-1.02)
PPV	0.70 (0.54-0.86)	0.56 (0.39-0.73)	0.91 (0.81-1.01)‡
NPV	0.83 (0.70-0.96)	0.93 (0.84-1.02)	0.95 (0.88-1.02)

Numbers in parentheses are 95% confidence intervals.
CT, Computed tomography; *PET,* positron emission tomography; *PPV,* positive predictive value; *NPV,* negative predictive value.
*$P < .05$, FDG-PET vs CT for sensitivity.
†$P < .05$, FDG-PET (focal) vs FDG-PET (positive) for specificity.
‡$P < .05$, FDG-PET (focal) vs FDG-PET (positive) for PPV.

postoperative course after reconstruction of the aorta. Other scintigraphic studies, including white blood cell or leukocyte scans, also showed a certain number of false-positive results.[21,22] This inevitable reaction might confound the critical diagnosis of aortic graft infection. However, these normal inflammatory reactions might be distinguished from infection by using the characteristic uptake patterns of FDG as diagnostic criteria, because nonspecific inflammation was associated with diffuse uptake along the prosthetic graft, whereas true infection was associated with focal or segmental FDG uptake, mostly at sites of abnormal CT findings. In this study, eight cases showed various degrees of false-positive FDG uptake, but the pattern of uptake was diffuse along the prosthetic graft in all cases. This feature can be a useful marker for differentiating between infected and noninfected aortic grafts. In fact, using focal uptake as a diagnostic criterion resulted in a statistically significant increase in the specificity and PPV of FDG-PET for the diagnosis of graft infection as compared with that of the conventional visual assessment. Using this focal sign may not always be versatile, because some grafts are entirely infected. In this type of infection, the focal findings do not work and cause misdiagnosis. We emphasize that the use of a combination of intensity and pattern of FDG uptake with reference to the information of CT scans may allow one to clearly distinguish between infected and noninfected aortic grafts. More extensive clinical evaluation is warranted to determine the accuracy of this method.

Recently, a fusion technology between FDG-PET and CT, acquired in a single session, has been developed that enables precise localization of any abnormal FDG uptake.[23,24] This hybrid PET/CT method is expected to become increasingly popular in the field of nuclear medicine, because FDG-PET always requires anatomic information for accurate localization of any abnormal tracer distribution. We could not use PET/CT in our present study, but a few case reports have confirmed the feasibility of PET/CT for the diagnosis of vascular prosthesis infection.[5,7] An incremental benefit of PET/CT over PET alone can be expected, but further studies should be undertaken to determine the role of FDG-PET/CT in the diagnosis of vascular prosthesis infection.

In this preliminary study, there were some limitations. First, the inability to confirm infection in these patients and, thus, have a gold standard is a fundamental problem in our attempt to test the diagnostic performance of FDG-PET. In cases in which no surgical treatment was available, follow-up CT and FDG-PET examinations were performed until the patient's fever, C-reactive protein levels, and positive blood cultures returned to the average level. However, it remains unsolved whether true infection existed in cases with FDG-PET–positive but CT-negative results in this study. Although vascular graft infection is rare complication, further studies including a larger population of precisely diagnosed graft infections are required. Second, we excluded patients with diabetes mellitus because this condition can affect the distribution of FDG uptake.[10] Although extensively assessed in patients with malignancies, the effect of hyperglycemia on FDG uptake by inflammatory and infectious processes is not well documented, and the effect of increased glucose serum levels on PET sensitivity is a controversial issue.[25-27] Accordingly, we tested the feasibility of FDG-PET in patients without diabetes mellitus. Recently, Keidar et al[28] have tested the role of FDG-PET/CT in the diagnosis of diabetic foot osteomyelitis. In their study, although increased serum glucose values were found in half of the study population, this did not lead to false-negative results. Because the large numbers of patients with vascular prosthesis have overt diabetes mellitus, further studies should be carried out to determine the feasibility of FDG in the diagnosis of vascular prosthesis infection in such patients. Third, approximately 75% of the patients had received antibiotics before CT and PET in this study. It was anticipated that antibiotic therapy before PET scanning would have some effect on the individual "false-negative" findings. In our study, both PET and CT scans might be equally influenced by antibiotics because medication started before and did not change throughout the imaging studies. Thus, the comparison between the two modalities is thought to be reliable. Fourth, PET is substantially more expensive than CT.[29-31] We did not have enough data to test the cost-effectiveness of FDG-PET for infectious diseases because the use of PET in this clinical field has just started. It would be expected that PET can

reduce unnecessary invasive procedures and save health care costs when used appropriately in the management of patients with infected aortic grafts. To prove this, further studies are necessary.

In conclusion, FDG-PET seems to be a promising modality for the evaluation and management of infected aortic grafts and may serve as a useful tool for noninvasive diagnosis of this clinical problem. Moreover, FDG-PET shows a diagnostic performance superior to that of CT when specific uptake patterns of FDG are included in the diagnostic criteria.

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